FORM PTO-1449 Atty Docket No. U.S. Dept. of Commerce Serial No. P1405R1C1 not assig Patent and Trademark Office Applicant LIST OF DISCLOSURES CITED BY APPLICANT de Sauvage et al. Filing Date (Use several sheets if necessary) Group 20 Nov 2001 **U.S. PATENT DOCUMENTS** Examiner Initials Date **Document Number** Name Class Subclass Filing Date 09/031,563 shang et al. de Saurage et al. 26.02.98 2 4,816,567 RH 28.03.89 Cabilly et al. 5,225,539 06.07.93 Winter, G. **FOREIGN PATENT DOCUMENTS** xamine Translation Initials Document Number Date Class Subclass Country Yes No EP 0 879 888 25.11.98 EPO 5 WO 95/18856 13.07.95 WO 96/11260 18.04.96 PCT WO 97/45541 04.12.97 PCT WO 99/29854 17.06.99 OTHER DISCLOSURES (Including Author, Title, Date, Pertinent Pages, etc.) Alcedo et al., "The Drosophila smoothened Gene Encodes a Seven-Pass Membrane Protein, a Putative Receptor for the Hedgehog Signal" Cell 86:221-232 (1996) RKY Apelqvist et al., "Sonic hedgehog directs specialised mesoderm differentiation in the intestine and pancreas* Current Biology 7(10):801-804 (Oct 1, 1997) Bellusci et al., "Involvement of Sonic hedgehog (Shh) in mouse embryonic lung growth and morphogenesis *11 <u>Development</u> 124(1):53-63 (Jan 1997) Bitgood et al., "Hedgehog and Bmp genes are coexpressed at many diverse sites of cell-cell interaction in the mouse embryo" <u>Developmental Biology</u> 172(1):126-138 (Nov 1995) *12 Bitgood et al., "Sertoli Cell Signaling by Desert Hedgehog Regulates the Male Germline" Current Biology 6(3):298-304 (1996) 13 Bowie et al., "Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions" 14 Science 247:1306-1310 (1990) Carpenter, D. et al., "Characterization of two patched receptors for the vertebrate hedgehog protein family" Proc. Natl. Acad. Sci. USA 95(23):13630-13634 (1998) Chen and Struhl, "Dual roles for patched in sequestering and transducing Hedgehog" Cell 87(3):553-563 (Nov 1, 1996) *16 Echelard et al., "Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity Cell 75:1417-1430 (1993) 17 Ericson et al., 'Sonic hedgehog induces the differentiation of ventral forebrain neurons: a common signal for ventral patterning within the neural tube" Cell 81(5):747-756 (Jun 2, 1995) 181 Fan et al., "Patterning of mammalian somites by surface ectoderm and notochord: evidence for sclerotome induction by a hedgehog homolog" Cell 79(7):1175-1186 (Dec 30, 1994) . 19 Fujiwara et al. (GenBank Accession No. D60589) (May 21, 1996) *20 Gailani et al., "The role of the human homologue of Drosophila patched in sporadic basal cell RKH *21 carcinomas" Nature Genetics 14:78-81 (Sept 1996) Examiner < **Date Considered** Examiner: Initial if reference considered, whether or not citation is in conformance with MPEP 609; draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

FORM PTO-1449		U.S. Dept. of Commerce	Atty Docket No.	Serial No.		
		Patent and Trademark Office	P1405R1C1	not assigned		
LIST OF	DISCLOSURES CITED BY APPLICANT	•.	Applicant de Sauvage et al.			
(Use several sheets if necessary)			Filing Date	Group		
 	materials of the state of the s		20 Nov 2001	1		
	·	RES (Including Author, Title, Date,				
PKH +2:		Genes Dev. 10(3):301-312 (1996)			
*2.						
*24	Hynes et al., "Control of cell patte oncogene Gli-1" Neuron 19(1):15-26 (e zinc finger transc	ription factor and		
*2	Johnson et al., "Ectopic expression of Sonic hedgehog alters dorsal-ventral patterning of somites" Co 79:1165-1173 (1994)					
+20	Johnson et al., "Human Homolog of Patched, a Candidate Gene for the Basal Cell Nevus Syndrome" Science 272:1668-1671 (1996)					
· +2	Jones, P.T. et al., "Replacing the Complementarity-determining Regions in a Human Antibody with Those From a Mouse" Nature 321:522-525 (May 29, 1986)					
*28	Krauss et al., "A functionally conserved homolog of the Drosophila segment polarity gene hh is exprein tissues with polarizing activity in zebrafish embryos" Cell 75:1431-1444 (1993)					
+29	g cascade and feedba 3-1003 (Dec 16, 1994					
*30	Marigo et al., "Biochemical evidence that patched is the Hedgehog receptor" Nature 384(6605):176-179 (Nov 14, 1996)					
* 3:	Marigo et al., "Conservation in hedgehog signaling: induction of a chicken patched homolog by hedgehog in the developing limb" <u>Development</u> 122:1225-1233 (1996)					
*32	Marti et al., "Requirement of 19K fo 2 CNS explants" Nature 375(6529):322-3		duction of distinct	ventral cell types		
*33	Morrison et al., "Chimeric Human Ant Region Domains" <u>Proc. Natl. Acad. Sc</u>			with Human Constant		
*34	Motoyama et al., "Ptch2, a second mo Genetics 18(2):104-106 (Feb 1998)	use Patched gene is co-expr	essed with Sonic hed	gehog' <u>Nature</u>		
RKH "35	Nakano et al., "A protein with sever segment polarity gene patched." Natur	al possible membrane-spanni <u>e</u> 341:508-513 (1989)	ng domains encoded b	y the Drosophila		
	Ngo et al., "The Protein Folding Problem and Tertiary Structure" pps. 492-495					
*36						
2KH -37	Nusslein-Volhard et al., "Mutations Affecting the Pattern of the Larval Cuticle in Drosophila Melanogaster" Roux's Archives of Developmental Biology 193(5):267-282 (1984)					
	Oro et al., "Basal cell carcinomas in mice overexpressing sonic hedgehog" <u>Science</u> 276(5313):817					
*39	Perrimon, N., "Hedgehog and Beyond"	Cell 80:517-520 (1995)				
*40	Presta, L., "Antibody Engineering" Curr. Op. Struct. Biol. 2:593-596 (1992)					
RKH "41	Rassoulzadegan et al., "Transmeiotic 1 (Dec 3, 1993)	differentiation of male gen	cm cells in culture	Cell 75(5):997-1000		
Examiner			ite Considered			

	*4.DTO	410 D	4 56 5 (Coriol No.			
FOH	FORM PTO-1449 U.S. Dept. of Commerce		Atty Docket No.	Serial No.			
•	*** * * * * * * * * *	Patent and Trademark Office	P1405R1C1	not assigned			
LIS	T OF D	SCLOSURES CITED BY APPLICANT	Applicant de Sauvage et al.				
	Graup						
(Use several sheets if necessary)		Filing Date 20 Nov 2001	Group 1				
		ATIES BOAL SUIDES (L. L. L	<u> </u>	<u> </u>			
		OTHER DISCLOSURES (Including Author, Title, Date,					
all	42	Riddle et al., "Sonic hedgehog mediates the polarizing activity	of the ZPA <u>Cell</u> :	5:1401-1416 (1993)			
KAII		7	*				
- 1	+43	Riechmann, L. et al., "Reshaping Human Antibodies for Therapy."	Nature 332:323-329	(Mar 24, 1988)			
1:		Debarba at all lifes to be a life and a life					
	*44	Roberts et al., "Sonic hedgehog is an endodermal signal inducin and regionalization of the chick hindgut" <u>Development</u> 121:3163-	3174 (1995)				
	+45	Stone et al., "The tumour-suppressor gene patched encodes a can Nature 384(14):129-134 (Nov 1996)	didate receptor for	Sonic hedgehog"			
1	*46	Summersgill et al., "Molecular cytogenetic analysis of adult te identification of regions of consensus copy number change" Brit	sticular germ cell t ish Journal of Cance	umours and er 77(2):305-313 (1998)			
-	-	Symth et al. Human Molecular Genetics 8(2):291-297 (1999)					
	*47						
	*48	Takabatake, T. et al., "Hedgehog and patched gene expression in 410:485-489 (1997)		*			
\exists	*49	Vortkamp et al., "Regulation of rate of cartilage differentiati protein" <u>Science</u> 273:613-622 (1996)		*			
	*50	Wallis, G., "Bone growth: Coordinating chondrocyte differentiat (1996)	ion" <u>Current</u> Biology	6(12):1577-1580			
	*51	Wicking and Bale, "Molecular basis of the nevoid basal cell car Pediatrics 9:630-635 (1997)	cinoma syndrome" <u>Cur</u>	rent Opinion in			
	*52	Xie et al., "Activating Smoothened mutations in sporadic basal- (Jan 1, 1998)	cell carcinoma" <u>Natu</u>	re 391(6662):90-92			
	* 53	Xie et al., "Mutations of the PATCHED gene in several types of Research 57(12):2369-2372 (Jun 15, 1997)	sporadic extracutane	ous tumors" <u>Cancer</u>			
	*54	Zaphiropoulos, P.G. et al., "PTCH2, a novel human patched gene up-regulated in basal cell carcinomas" Cancer Research 59:787-7	undergoing alternati 92 (1999)	ve splicing and			
	1	de Jong et al., "Pathogenesis of adult testicular germ cell tum		odoli. Concon Constituti			
	+55	& Cytogenetics 48(2):143-167 (Sep 1990)	ors. A cycogenetic w	cancer Generals			
4-	-	van den Heuvel and Ingham, "Smoothened Encodes a Receptor-Like"	Sermentine Protein R	emired for Hedgehog			
RH	*56	Signalling" Nature 382:547-551 (1996)		edutied for nedgenoy			
1441	-		****				
	-						
	1						
-			<u> </u>				
	1						
Examin	ner) () () () Da	ate Considered				
	Kally K. Hamuett 12/14/04						
*Exam	iner: In	tial if reference considered, whether or not citation is in conformance with MPEP	609; draw line through cit	ation .			